REMARKS/ARGUMENTS

Status

Claim 57 is pending in the application.

Applicants thank the Examiner and Supervising Examiner for the interview on October 23, 2008 in which the pending claim and obviousness rejection were discussed. The Supervising Examiner had also indicated that the Examiner would speak to an examiner in the quality assurance group. The Examiner's conversation with the quality assurance group was discussed in a follow up phone interview on November 5, 2008. The Examiner agreed to further consider the cited art in light of Applicants' evidence of surprising results.

Applicants respectfully request that the Examiner also provide an official Interview Summary.

Rejection under 35 U.S.C. § 103

Claim 57 remains rejected as allegedly obvious over a combination of ten references, two of which are Shen *et al., Int. J. Cancer* 42:792-797, 1988 ("Shen") and Ghetie *et al., Cancer Res.* 51:5876-5880, 1991 ("Ghetie"). Applicants disagree with the Examiner's legal conclusions for reasons of record. The cited art does not lead to an expectation of clinical efficacy at the level achieved with an immunoconjugate as claimed. Applicants respectfully request that the Examiner consider the following comments with regard to Shen and Ghetie.

First, Shen's experiments relate to the immunotoxin conjugates IgG-RFB4-A and Fab'-RFB4-A. These two immunotoxins are prepared with the A chain of ricin, not with PE, (see, *e.g.,* the first line of the abstract, and paragraphs 1 and 2 on page 792) that is linked to RFB4-Fab' or RFB4 IgG, not to RFB4dsFv. It is these particular ricin A chain immunoconjugates that are described by Shen as having potent cyotoxicity (see, for example page 796, referring to IgG-RFB4-A or Fab'-RFB4-A). Shen only indicates that these particular immunoconjugates are candidates for clinical trials in general. Moreover, Shen evaluates cytotoxic activity of the immunoconjugates on cells *in vitro*. The cells Shen employs are a Burkitt lymphoma cell line, a myeloma cell line, and a pre-B-cell leukemia (last paragraph,

second column, page 793). Shen's results thus relate to use of a different imunotoxin in experiments performed only *in vitro* on cell lines that are not hairy cell leukemia cells. Accordingly, the disclosure in Shen simply does not provide a basis that would lead one of skill to the conclusion that treatment of patients who have hairy cell leukemia with an immonconjugate as claimed could achieve a complete remission.

Ghetie has also been cited in the obviousness rejection. Ghetie shows that the RFB4 IgG and RFB4Fab' immunotoxins made with deglycosylated ricin A-chain (dgA) are cytotoxic *in vivo* in a mouse model of B-cell lymphoma, not hairy cell leukemia. Most of Ghetie's experiments compared the antitumor effect of the two immunotoxins under conditions in which the tumor cell burden is minimal (page 5879, column 1, the last sentence bridging to column 2). Although in one experiment the intact RFB4 IgG-ricin A toxin was administered at a late stage of tumor growth (Table 4, page 5878), there is no teaching or suggestion that any of these animals went into complete remission, or that the authors would expect to achieve complete remission in patients who were administered their immunotoxins. Thus, the teachings in Ghetie also cannot serve as a basis for predicting the level of efficacy that was achieved using RFB4dsFv-PE38 in a Phase I clinical trial for the treatment of hairy-cell leukemia.

The current claim reflects the context in which Applicants' surprising results were obtained. The evidence of record of superior results therefore properly supports the nonobviousness of the claims. Accordingly, Applicants request withdrawal of the rejection.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance and an action to that end is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 415-576-0200.

Respectfully submitted,

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